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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/358,937	07/23/1999	ALLAN C. SPRADLING	PM 254812	2149

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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

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23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/358,937	Applicant(s) Spradling, A.C. et al.
	Examiner Joseph Woitach	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Jan 16, 2003*.

2a) [X] This action is **FINAL**. 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-8, 11-49, and 51* is/are pending in the application.

4a) Of the above, claim(s) *3, 19-22, 32, and 34* is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1, 2, 4-8, 11-18, 23-31, 33, 35-49, and 51* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [X] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [X] Notice of References Cited (PTO-892)	4) [ ] Interview Summary (PTO-413) Paper No(s).
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) [ ] Notice of Informal Patent Application (PTO-152)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s).	6) [ ] Other:

DETAILED ACTION

This application is an original application filed July 23, 1999 which claims benefit to provisional application 60/094,008, filed July 24, 1998.

Applicants' amendment filed January 16, 2003, paper number 22, has been received and entered. Claim 50 has been canceled. Claims 33 and 41 have been amended. Claim 51 has been added. Claims 1-8, 11-49 and 51 are pending.

Election/Restriction

Claims 1-8, 11-49 and 51 are pending. Claims 3, 19-22, 32 and 34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1, 2, 4-8, 11-18, 23-31, 33, 35-49 and 51 are currently under examination.

This application contains claims drawn to an invention nonelected with traverse in Paper No. 11. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Response to Amendment

The declaration of Allan C. Spradling made under 37 CFR 1.132 filed January 16, 2003, paper number 21, is sufficient to overcome the rejection of claims 1, 2, 4-8, 11-18, 23-31, 33, 35-49 based upon 35 U.S.C. 102(b) over Twombly *et al.* and Forbes *et al.* and 35 U.S.C. 103 over Twombly *et al.* and Forbes *et al.* in view of Lin *et al.*

The declaration will be discussed in greater detail as it applies to basis of the rejections set forth below.

Claim Objections

Claim 33 objected to because the only two steps recited are labeled (c) and (d) and does not consist of initial method steps (a) and (b) is withdrawn.

Amendments to the claim has obviated the basis of the objection.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly amended claim 40 and newly added claim 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such

a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Specifically, the recitation of 'a GAL4 driver ' is considered new matter. Upon review of the specification pointed to by Applicants for support of the amendment, page 18, lines 22-23 and 33, no literal support for GAL4 driver is recited. Further, the specification recites and teaches only specific expression constructs are used to express and provide *dpp* to the fly. Finally, in light of the arguments presented in the declaration of Allan C. Spradling, the promoter and expression system appears to be critical in obtaining the phenotype of an increased stem cell population in transgenic flies. Because there is not literal support for GAL4-driver, and the evidence of record indicates that the promoter is critical to practicing the claimed invention, there is no figurative to support altering the promoter from that specifically disclosed in the instant specification to any other promoter that would be generally known in the art.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 40 and 51 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

Claims 1, 2, 4-8, 11-18, 23-31, 33, 35-49 and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing the abundance of germline stem cells of Drosophila *in vivo* comprising: (a) providing a population of germline stem cells in a female host transgenic Drosophila wherein the transgenic Drosophila ectopically expresses Dpp wherein said ectopic expression of Dpp is in germanium cells using hsp70-GAL4 and the UAS-dpp (set forth in Band and Perrimon, 1993); and (b) subjecting the germaria of the female host transgenic Drosophila to heat shock; wherein the heat shock

stimulation increases the abundance of germline stem cells as compared to a population wherein the germaria of the female host transgenic Drosophila was not subjected to heat shock, does not reasonably provide enablement for the use of any other transgenic Drosophila or practice in any other organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the specification provides the general guidance that by stimulating the BMP signaling pathway, in particular providing BMP-2/4 or the homolog dpp, allows for the propagation of stem cells in an undifferentiated state (page 1, lines 10-19). The working examples provide one specific transgenic construct for providing the ectopic expression of Dpp in a transgenic fly. Other transgenic flies are taught wherein other transgenes are expressed and complementary receptors which are knock-outed are analyzed, however all are provided in part to demonstrate that ectopic expression of Dpp increases the number germline stem cells. Previously, a rejection made under 35 U.S.C. 102 over the teachings of Forbes *et al.* and Twombly *et al.* was made because these references teach transgenic flies which meet the structural limitations encompassed by the claims. However, in the declaration of Dr. Spradling, evidence is provided which indicates that the transgenic flies which produce Dpp in the germaria while producing increased number of germline cells do not produce an increased abundance of germline stem cells. In light of this evidence and the general guidance provided by the specification it is unclear what particular method of stimulation will specifically affect the claimed outcome of increasing the abundance of germline stem cells beyond the specific example disclosed.

The art of transgenics is not a predictable art with respect to transgene behavior. Without evidence to the contrary, transgene expression in different species of transgenic non-human animals is not predictable and varies according to the particular host species. This observation is specifically supported by Hammer *et al.* who report the production of transgenic mice, sheep and

pigs; however, only transgenic mice exhibited an increase in growth due to the expression for the gene encoding human growth hormone (pages 276-277). The same transgene construct in transgenic pigs and sheep did not cause the same phenotypic effect. Ebert *et al.* report a transgenic pig that did not develop an expected phenotype of growth during the rapid growth phase, when transfected with a Moloney murine leukemia virus rat somatotropin fusion gene (p. 277, summarized in abstract). The observation is further supported by Mullins *et al.* who report on transgenesis in the rat and larger mammals. Mullins *et al.* state that "a given construct may react very differently from one species to another" (see Summary section). Wall *et al.* further report that "transgene expression and the physiological consequences of transgene products in livestock are not always predicted in transgenic mouse studies" (page 62, first paragraph). The art as noted in the instant specification teaches that the prior art has failed to identify and characterize factors involved in germline stem cell maintenance and propagation (page 4, liens 7-10). Given species differences in the expression of various transgenes, in particular the TGF-β super family members, one of skill in the art would have been required to undergo undue experimentation to determine which promoters and specific transgene constructs would produce the desired phenotype in all non-human animals. In the instant case, the specific elements used in the construction of the DNA plasmids for use in generating the transgenic animals were not discovered by Applicant, rather they were derived from the art based on reports of their function in mice. Absent of evidence to the contrary, it is not clear that these elements would be functional in other animal species in the same manner as they have been demonstrated in the

transgenic fly. Further, given that other related members of the TGF-β super family result in different phenotypes in various species of animals, there is no expectation that the phenotype observed for the transgenic Drosophila disclosed in the instant specification would extend to other organism.

Additionally, while the state of the art of transgenics is such that one of skill in the art would be able to produce transgenic animals comprising a transgene of interest, it is not predictable if the transgene would be function at a level and specificity sufficient to cause a particular or specific phenotype. The art of transgenics is not a predictable art with respect to transgene behavior or resulting phenotype. Without evidence to the contrary, transgene expression in different species of transgenic non-human animals is not predictable and varies according to the particular host species and to the transgene used. This observation is specifically supported by Hammer *et* al. who report the production of transgenic mice, sheep and pigs; however, only transgenic mice exhibited an increase in growth due to the expression for the gene encoding human growth hormone (pages 276-277). The same transgene construct in transgenic pigs and sheep did not cause the same phenotypic effect. Similarly, Ebert *et al.* report a transgenic pig that did not develop an expected phenotype of growth during the rapid growth phase, when transfected. Further, as noted above, McPherron *et al.* teach that expression of mutant forms of other TGF-β super family members result in phenotypic differences among the species examined (page 12460). However, while a redundancy may make a particular member of a the TGF-β super family dispensable in some cases, this does not simply extend to all types

of alterations in the TGF-β super family or particular phenotypes produced by said alterations. For example, Yamaoka *et al.* (1998) teach that two alterations of TGF-β which should result in a null phenotype, over-expression of a TGF-β dominant negative mutant and a TGF-β knockout construct, result in different affects on acinar cells in the pancreas (page 300, middle of first column). Thus, in view of the art even the expression of two different transgenes from the TGF-β superfamily which should result in the same affect result in different phenotypes *in vivo* when expressed as transgenes.

Finally, the claims as written reads on stimulating Dpp by any means and more specifically in transgenis on use of any promoter, however in light of the evidence provided in the declaration of Dr. Spradling, it is unclear which if any construct would provide the necessary expression of Dpp besides that explicitly disclosed. The specification fails to provide the necessary guidance with regard to a promoter other than that disclosed in Example 1, page 16. Again, the art of transgenics is not a predictable art with respect to promoters and expression vectors. Without evidence to the contrary, transgene expression in different species of transgenic non-human animals is not predictable and varies according to the specific promoter/gene combination(s). The specific promoter used and the specific cDNA used could be important in determining the resulting phenotype. Wall generally supports the observation by stating that "our lack of understanding of essential genetic control elements makes it difficult to design transgenes with predictable behavior." (see page 61, last paragraph). While the state of the art of transgenics is such that one of skill in the art would be able to produce transgenic animals

comprising a transgene of interest, it is not predictable if the transgene would be expressed at a level and specificity sufficient to cause a particular phenotype. The individual gene of interest, promoter, enhancer, coding, or non-coding sequences present in the transgene construct are all important factors in controlling the expression of the transgene. In the instant case, because the art teaches that the phenotypic affect of Dpp as set forth in Twombly *et al.* and Forbes *et al.* and as evidenced by the declaration of Dr. Spradling requires more than simply providing Dpp in the correct cells of the transgenic fly, the specification fails to describe any other promoter besides that specifically used in working example 1.

As discussed above, the claims are broad, encompassing any organism by simply stimulating Dpp expression by any means. Further, while narrow embodiments are set forth for the use of transgenic Drosophila, in light of the unpredictability of transgene behavior and resulting phenotype and the evidence present by Dr. Spradling it is unclear to whether the artisan can extend the observation presented in the instant specification to the use of any other transgenic construct. The courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. 27 USPQ2d 1662 *Ex parte Maizel.* Scope of Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). In view of the quantity of experimentation necessary to determine the parameters listed above, the lack of direction or guidance provided by the specification, the absence of working examples for the demonstration or correlation to the production of transgenic animal models of any species, or other promoters which broadly meet the functional language

encompassed by the claims, and the general unpredictable state of the art with respect to the generation of transgenic animals of all species, it would have required undue experimentation for one skilled in the art to make and/or use the claimed inventions as broadly claimed.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

Claim 40 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

First, it is noted that the claim has been amended to encompass a 'GAL4 driver'. The amendment to the claim from encompassing a specific promoter not adequately described in the present disclosure to one encompassing a general promoter has obviated the basis of the rejection over the embodiment of 'hsp70-GAL4' however the claims still encompass 'UAS-*dpp*'. Further, the claims still require that a GAL4 driver capable of driving expression of the UAS-dpp be provided, wherein these two sequences are capable of producing increased stem cell in flies when expressed. Applicants argue that 'UAS-*dpp* in the claim refer generically to any UAS-*dpp* construct and not any specific construct'. Further, Applicants note that the GAL4-UAS system was known and used by many in the art prior to the practice of the invention, and need not attest

to the public availability. Finally, Applicants note that Drosophila stocks employed in the working examples in the specification may be obtained form the Bloomington Stock Center. See Applicants' amendment, page 4, Section A. Applicants' arguments have been fully considered, but not found persuasive.

Amended claim 40 and claim 51 are directed to ectopic expression of Dpp with a GAL4 driver and UAS-dpp. It is noted that various fly stocks comprising various transgenes are publicly available, for example as those provided by the Bloomington Stock Center. However, the instantly claimed invention is directed to specific gene constructs in a fly whose expression produces a specific phenotype in a transgenic fly. There is no evidence of record that the specific transgenic fly(s) required to practice the claimed invention are publicly available. Further, as discussed in the declaration of Allan C. Spradling, paper number 21, not all transgenic flies, such as those set taught in Twombly *et al.* and Forbes *et al.*, which are capable of providing dpp in the correct cells and area of the fly will produce the phenotype of increasing the number of stem cells as required in the preamble and final step of the independent claim. Given that the hsp promoter is used to drive expression of transgenes in both the working examples and the examples provided by in Twombly *et al.* and Forbes *et al.*, it appears a critical and required transgene construct/system is necessary to achieve the claimed phenotype in the resulting transgenic fly. As noted in the previous office action the hsp70-GAL4 and UAS-dpp are vectors which used to express dpp (see page 16, lines 14-15 in Example 1). It is noted that immediately following the recitation of the vectors, the specification cites Brand and Perrimon, 1993, apparently in

reference to these vectors. The reference of Brand and Perrimon is not presently made of record, and upon review of the present disclosure, there is no other support for the specific elements or characteristics of polynucleotide sequences for hsp70-GAL4 and UAS-dpp taught in the present specification. In light of Applicants arguments presented in the declaration of Allan C. Spradling, the expression of the transgene is critical in practicing the instantly claimed method and obtaining the claimed phenotype of an increased stem cell population. Thus, the single working example provided in the present specification appears to be critical to practicing the instantly claimed method, and since the GAL4 driver (i.e. the hsp70-GAL4 sequences) and UAS-dpp are specifically set forth in the claim they are essential to practice the claimed invention. In order to satisfy the requirements of 35 U.S.C. 112, first paragraph, the invention must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. In this case if the specific vectors or the resulting flies made with said vectors are not so obtainable or available, the requirements of 35 U.S.C. 112, regarding "how to make", may be satisfied by a deposit of vectors. As previously noted the specification indicates that the vectors disclosed and used in the specification were first taught in Brand and Perrimon, 1993, but there is no indication in the specification as to public availability of these sequences (specification page 16). Further, there is no evidence that the resulting transgenic flies comprising these vectors and demonstrating the phenotype of increased population of stem cells were publicly available. If the sequences or the transgenic flies were made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of

record over his or her signature and registration number, stating that the specific cell lines have been deposited under the Budapest Treaty and that the cell lines will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement.

It the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request of for the effective life of the patent, whichever is longer; and,

(d) a test of viability of the biological material at the time of deposit (see 37 CFR 1.807); and,

(e) the deposit will be replaced if it should ever become inviable.

Therefore, for the reasons above and of record, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 46 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

The cancellation of claim 50 has obviated the basis of the rejection.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-8, 11-18, 23, 24, 28-31, 33, 35-39 and 41-49 rejected under 35 U.S.C. 102(b) as being anticipated by Twombly *et al.* is withdrawn.

Claims 1, 2, 4-8, 11-18, 23, 24, 28-31, 33, 35-39 and 41-49 rejected under 35 U.S.C. 102(b) as being anticipated by Forbes *et al.* is withdrawn.

Applicants argue that the transgenic flies taught in Twombly *et al.* and Forbes *et al.* demonstrate and increase in germline cells, but not germline stem cell. Further, it is argued and noted that the transgenic flies taught by Twombly *et al.* and Forbes *et al.* have been analyzed by

Dr. Spradling's laboratory and that said transgenic flies do not demonstrate an increase abundance of germline stem cells. The evidence of Dr. Spradling's experiments using the transgenic flies of Twombly *et al.* and Forbes *et al.* is presented in a declaration filed under 37 CFR 1.132 (paper number 21). See Applicants' amendment, pages 5-7, Section C and Declaration of Allan Spradling. Applicants' arguments and declaration have been fully considered and found persuasive.

Because the claims have been amended to recite that the practice of the method results in increased abundance of germline stem cells, encompassing a different and unexpected result over that disclosed by Twombly *et al.* and Forbes *et al.* applicants arguments and evidence is found persuasive, and the rejection is withdrawn. It is noted that in the teaching of Twombly *et al.* and Forbes *et al.* the transgenic flies meet the structural limitations set forth in independent claim 1 and that unexpected results are not sufficient to overcome a rejection made under 35 U.S.C. 102. However, in light of the evidence presented by Dr. Spradling the rejection is withdrawn.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 25-27 rejected under 35 U.S.C. 103(a) as being unpatentable over either Forbes *et al.* or Twombly *et al.* and Lin *et al.* is withdrawn.

As argued in traverse of the rejection made under 35 U.S.C. 102(b), Applicants argue that the transgenic flies taught in Twombly *et al.* and Forbes *et al.* demonstrate and increase in germline cells, but not germline stem cell. Further, it is argued and noted that the transgenic flies taught by Twombly *et al.* and Forbes *et al.* have been analyzed by Dr. Spradling's laboratory and that said transgenic flies do not demonstrate an increase abundance of germline stem cells. The evidence of Dr. Spradling's experiments using the transgenic flies of Twombly *et al.* and Forbes *et al.* is presented in a declaration filed under 37 CFR 1.132 (paper number 21). See Applicants' amendment, pages 7-8, Section D and Declaration of Allan Spradling. Applicants' arguments and declaration have been fully considered and found persuasive.

Conclusion

No claim is allowed. The claims are free of the art of record because while the art teaches transgenic flies which are encompassed by the metes and bounds of the claims, the newly

provided evidence by Dr. Spradling differentiates the teachings of prior art from that which is instantly claimed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Joseph T. Woitach

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800/1632